REMARKS

1. Status

Claims 44-50 and 52-56 are currently pending, claim 44 has been amended.

2. Support for Amendments

Support for the amendment to claim 44 can be found *inter alia* on page 87, line 10- page 88, line 9; page 88, line 10- page 89, line 3; page 89, line 4- page 90, line 3; as and page 71, line 3- page 72, line 11. No new matter has been added as a result of the instant claim amendments.

3. Rejections under 35 U.S.C. § 112, second paragraph

Claims 44-50 and 52-56 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

35 U.S.C. § 112, second paragraph requires "the specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."

The Patent Office asserts that claim 44, which recites "wherein the program results are displayed to a user" lacks antecedent basis for "the program results." Claim 44 has been amended, thereby obviating the rejection. As noted by the Patent Office claim 45-50 and 52-56 are rejected due to their dependence on claim 44, thus the amendment to claim 44 obviates the rejection of the dependent claims as well. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection.

4. Rejection under 35 U.S.C. § 102 (b)

Claims 44-49, 53 and 56 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Kamentsky et al. (US 5,427,910). The Applicants traverse the rejection.

According to M.P.E.P. 2131, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The Patent Office asserts that the amendment to claim 44 which recited "the first cellular compartment and the second cellular compartment are different" and was made in the previous response filed 6-27-07 "is part of the preamble, and therefore has not been given patentable weight." Applicants note that the rest of claim refers back to this limitation in preamble and thus resulted in the limitation having patentable weight. However, in order to expedite prosecution, Applicants have amended the claim to recite this limitation in the body of the claim and not the preamble.

As noted by the Patent Office in the previous Office Action mailed March 16, 2007, "Kamentsky et al. teach a method of fluorescent cytogenetic analysis that provides for the optical detection of chromosomal abnormalities..." Kamentsky does not teach or suggest at least the following limitations of currently pending claim 44:

> A machine readable storage medium comprising a program containing a set of instructions for causing a cell screening system to execute procedures for detecting the translocation of a cellular component of interest between a first cellular compartment and a second cellular compartment on or within individual cells on an array of locations which contain multiple cells, wherein the procedures comprise:
>
> a) **defining a first cellular compartment mask and a second cellular compartment mask in multiple individual cells** on the array of locations from luminescent signals obtained from a plurality of luminescent reporter molecules on or in the individual cells, wherein the plurality of luminescent reporter molecules comprises at least a first luminescent reporter molecule capable of identifying the individual cells, and at least a second luminescent reporter molecule capable of reporting on a cellular component of interest, wherein luminescent signals from the at least first and the at least second luminescent reporter molecules are optically distinguishable **and wherein the first cellular compartment and the second cellular compartment are different**;
>
> b) **determining an intensity of the luminescent signals from the at least second luminescent reporter molecule in the first cellular compartment mask and the second cellular compartment mask; and**
>
> c) **determining one or both of the following:**
>
> **i) a ratio of the intensity of the luminescent signals from the at least second luminescent reporter molecule in the first cellular compartment mask and the second cellular compartment mask in individual cells**; and
>
> ii) **a difference of the intensity of the luminescent signals from the at least second luminescent reporter molecule in the first cellular compartment mask and the second cellular compartment mask in individual cells**;
>
> **wherein the ratio of the intensity of the luminescent signals from the at least second luminescent reporter molecule in the first cellular**

compartment mask and the second cellular compartment mask and/or the difference of the intensity of the luminescent signals from the at least second luminescent reporter molecule in the first cellular compartment mask and the second cellular compartment mask provides a measure of the translocation of the cellular component of interest between the first cellular compartment and the second cellular compartment on or within the individual cells, and

wherein program results are displayed to a user.

Specifically, Kamentsky teaches "...a method of characterizing the **chromosomes** in a sample of cells..." (Column 3, line 8). Even if the chromosomes in Kamentsky are considered cellular compartments, disclosure of detecting chromosomeal abnormalities does not teach or suggest "detecting the translocation of a cellular component of interest between a first and second cellular compartments, **where the first and second cellular compartments are different;**" nor of the further limitations recited in claim 44.

For example, Kamentsky does not teach or suggest taking a ratio or a difference of the intensity of the luminescent signals in the first and second cellular compartments masks (i.e. in **different** cellular compartments) as recited in claim 44. Kamentsky teaches determining the "distance between the labeled" chromosomes in order to "characterize the chromosomes in the cell sample." Thus, Kamentsky only discloses determining a distance between labels in chromosomes, not determining a difference or a ratio between a first and a second cellular compartment (i.e. **different** cellular compartments). Thus, Kamentsky does not anticipate amended claim 44. Claims 45-49, 53 and 56 are dependent on claim 44 and share the above limitations, and thus Kamentsky also does not anticipate claims 45-49, 53 and 56. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

5. Rejections under 35 U.S.C. § 103 (a)

A. Claims 44-50, 52, 53, and 56 are rejected under 35 U.S.C. 103 (a) as obvious over Mason et al. in view of Wright et al.

In order to establish a *prima facie* case of obviousness the Patent office must establish three criteria; 1) a suggestion or motivation found within the prior art or within the knowledge of one of skill in the art to combine or modify the references; 2) a reasonable

expectation of success; and 3) the prior art references alone or in combination must teach or suggest ***all*** the claim limitations. MPEP § 706.02(j).

The Patent Office asserts that Mason et al. teach a system which "provides a means for spatial digitization of cells (i.e. masking) [See Fig. 12.15 and Plate 29.1, for example], wherein pixel intensity profiling [See Fig. 12.16, Plate 29.1, and 29.2] and ratio analysis [Plate 13.2] are both used to compare spatial and temporal differences in the distribution (i.e. translocation) of fluorescent probes at a plurality of locations between different cellular compartments."

Contrary to the Patent Office's assertion, Mason et al. does not teach at least the following claim limitations of pending claim 44::

> A machine readable storage medium comprising a program containing a set of instructions for causing a cell screening system to execute procedures for detecting the **translocation of a cellular component of interest between a first cellular compartment and a second cellular compartment on or within individual cells on an array of locations which contain multiple cells,** wherein the procedures comprise:
>
> a) d**efining a first cellular compartment mask and a second cellular compartment mask in multiple individual cells** on the array of locations from luminescent signals obtained from a plurality of luminescent reporter molecules on or in the individual cells, wherein the plurality of luminescent reporter molecules comprises at least a first luminescent reporter molecule capable of identifying the individual cells, and at least a second luminescent reporter molecule capable of reporting on a cellular component of interest, wherein luminescent signals from the at least first and the at least second luminescent reporter molecules are optically distinguishable **and wherein the first cellular compartment and the second cellular compartment are different**;
>
> b) determining an intensity of the luminescent signals from the at least second luminescent reporter molecule in the first cellular compartment mask and the second cellular compartment mask; and
>
> c) **determining one or both of the following:**
>
> **i) a ratio of the intensity of the luminescent signals from the at least second luminescent reporter molecule in the first cellular compartment mask and the second cellular compartment mask in individual cells; and**
>
> **ii) a difference of the intensity of the luminescent signals from the at least second luminescent reporter molecule in the first cellular compartment mask and the second cellular compartment mask in individual cells;**
>
> **wherein the ratio of the intensity of the luminescent signals from the at least second luminescent reporter molecule in the first cellular compartment mask and the second cellular compartment mask and/or the**

difference of the intensity of the luminescent signals from the at least second luminescent reporter molecule in the first cellular compartment mask and the second cellular compartment mask provides a measure of the translocation of the cellular component of interest between the first cellular compartment and the second cellular compartment on or within the individual cells, and

wherein the program results are displayed to a user.

Specifically, Mason et al. does not teach, suggest or make obvious measuring translocation of a cellular component of interest between first and second cellular compartments of interest. Mason et al is a chapter in a guide book which generally addressed laboratory techniques for imaging of optical probes in living cells during quantitative PCR. Mason discloses a wide variety of general uses for imaging optical probes in whole cells, but not translocation between different cellular compartments in individual cells. For example, the images cited with particularity by the Patent Office, Fig. 12.16, Plate 29.1 and 29.2 demonstrate spread of fluorescence throughout the cell in response to stimulation and before, during and after photobleaching respectively. As stated in the figure and plate legends, Figure 12.16 "shows clearly the spread of the calcium wave along the cell," Plate 29.1 "show fluorescence before bleaching, immediately after the bleach and after recovery" in cells, and Plate 29.2 shows "images of cells prior to, immediately after and 16 min after photobleaching." The Figures and Plates disclosed in Mason, including those cited by the Patent Office in the instant Action, do not teach measuring translocation of a cellular component of interest between a first and a second cellular compartment, where the cellular compartments are different, but rather teach imaging of a general spread of fluorescent molecules throughout the cell. Imaging the spread of fluorescent molecules throughout the whole cell as taught by Mason et al. is not the same as measuring the translocation of a fluorescent molecule between specific and distinct cellular compartments as recited in the instant claim. Thus, Mason et al also does not teach, suggest, or make obvious defining a mask of a first cellular compartment and a second cellular compartment wherein the first and second cellular compartments are different as recited in the instant claim. Nor does Mason teach, suggest, or make obvious determining the ratio or difference of the intensity of the luminescent signals in the first and second cellular compartments masks (i.e. in **different** cellular compartments) as recited in claim 44.

The Patent Office asserts that Wright et al "teach the use of confocal microscopy techniques for determining the intercellular distribution (i.e. translocation) of multiple fluorescent probes in plant cells [Abstract]." As noted by the Patent Office, Wright et al, teaches imaging the distribution of fluorescent probes between cells (intercellular—between different cells in a plant) Thus, similar to Mason et al. and as noted by the Patent Office, Wright et al. teach imaging the general spread of fluorescent molecules between cells and not translocation between different cellular compartments in individual cells as recited in claim 44. Thus, the combination of Mason et al. with Wright et al. does not cure the deficiencies of Mason et al. with respect to the claim limitations of claim 44. Wright et al. does not teach, suggest, or make obvious teach measuring translocation of a cellular component of interest between a first and second cellular compartment in individual cells, but rather teach imaging of a general spread of fluorescent probes between cells in order to follow the probes' movement through a plant. Thus, the combination of references cited by the patent office does not teach, suggest, or make obvious **all** of the limitations of claim 44. The rejected claims 45-50, 52, 53 and 56 are all dependent on claim 44, share the above limitations, and add further limitations that are not taught or suggested by the combination of references, and thus are not rendered obvious over the cited references.

B. Claims 44-50 and 52-56 are rejected under 35 U.S.C. 103 (a) as obvious over Taylor et al. in view of Bastiaens et al. and the legal decision of *In re Venner*.

Taylor et al. is a publication of an international application filed May 29, 1997 and published December 4, 1997. In order to determine the proper prior art date for a PCT application for use in a 35 U.S.C. 103 rejection, it is necessary to first determine under which 35 U.S.C. 102 provision the PCT application is being applied as prior art.

MPEP 1857.01 states:

> *An international >application< ** may be used as prior art as of its international filing date, or an earlier U.S. filing date for which ** benefit is properly claimed, under 35 U.S.C. 102(e) if the international application:*
>
> ***(A) was filed on or after November 29, 2000;***
> *(B) designated the United States; and*
> *(C) was published under PCT Article 21(2) in the English language.*
> [emphasis added]

The Taylor et al. references was not filed on or after November 29, 2000 and thus does not fulfill requirement (A), and therefore cannot be used as a 102(e) reference. MPEP 1857.01 goes on to state that:

> *If **any** of the above conditions have not been satisfied, the publication of the international application and the U.S. application publication of the national stage after compliance with 35 U.S.C. 371 may only be used as prior art as of its **publication date** under 35 U.S.C. 102(a) or (b).... In addition, international applications, which: (1) **were filed prior to November 29, 2000**, (2) did not designate the U.S., or (3) were not published in English under PCT Article 21(2) by WIPO, **may not be used to reach back (bridge) to an earlier filing date through a ** benefit claim for prior art purposes under 35 U.S.C. 102(e)**.* [emphasis added]

Thus, the 102(a) or (b) date of the Taylor et al reference is the publication date which is December 14, 2007. Thus, according to the MPEP, Taylor et al. may only be applied as prior art under 35 U.S.C. 102 and 103 as of its publication date, which is December 4, 1997. The applicant's priority date in the pending case is February 27, 1997 which is earlier than the publication date of the Taylor et al. reference. Thus, Taylor et al. is not a proper prior art reference as it is not prior art according the MPEP.

As further noted in the MPEP § 706.02(j):

> *In order to establish a prima facie case of obviousness the Patent office must establish three criteria; 1) a suggestion or motivation found within the prior art or within the knowledge of one of skill in the art to combine or modify the references; 2) a reasonable expectation of success; and 3) the prior art references alone or in combination must teach or suggest **all** the claim limitations.*

As acknowledged by the Patent Office in its combination of Taylor et al with Bastiaens et al., Bastiaens et al. does not teach or suggest all of the claim limitation of claim 44, and thus does not render claim 44 obvious. The rejected claims 45-50 and 52-56 are all dependent on claim 44 and thus are not rendered obvious over the cited references.

In re Venner is cited by the Patent Office in support of Taylor et al. The Patent Office asserts that *In re Venner* "indicates that automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish the prior art in

terms of patentability." The Patent Office does not assert that *In re Venner* teaches, suggests, or makes obvious any of the specific claim limitations of claim 44. Thus, given that Taylor et al. is not a proper prior art reference, *In re Venner* does not, by itself, or in combination with only Bastiaens et al. render claim 44 or any of the dependent claims obvious.

In summary, given that Taylor et al is not a proper prior art reference that patent Office has failed to establish a prima facie case of obviousness of claims 44-50 and 52-56 over Taylor et al in view of Bastiaens et al and *In re Venner*. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

Conclusion

Based on all of the above, the Applicants believe the claims are now allowable. If there are any questions or comments regarding this response, the Patent office is encouraged to contact the undersigned agent as indicated below.

Respectfully submitted,

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